## REMARKS

Claims 63-93 were pending in the present application. The Examiner has withdrawn claims 66-68 and claims 76-93 from consideration. By this Amendment, Applicants have amended claims 63 and 73 and have added new claims 94 and 95. Support for the claim amendments and the newly presented claims can be found throughout the specification and claims as originally filed. Specifically, support can be found, *inter alia*, at pages 3-5 of the specification and in particular, page 5, paragraph 2. The present Amendment does not introduce any new matter and thus, its entry is respectfully requested. Upon entry of the present Amendment, claims 63-65, 69-75, and 94-95 will be pending and under examination.

### The September 15, 2005 Office Action

Restriction Requirement

The Examiner has made the previously set forth Restriction Requirement final, but has modified it slightly to include claim 74 within the elected group.

Information Disclosure Statement

The Examiner stated that "[i]t is noted that the information disclosure statement of 03/11/02 could not be considered, because it is prior to the filing date of 06/17/02, and therefore has not been filed in this case."

In response, Applicants respectfully disagree with the Examiner's position and assert that the Information Disclosure Statement must be considered because it was properly filed within the

time periods set forth in 37 C.F.R. §1.197(b), in particular, 1.97(b)(3). Although the requirements of 35 U.S.C. §371 were not completed in the present application until June 17, 2002, (because the Declaration had not been submitted prior to that time), Applicants and Examiner both recognize that the Information Disclosure Statement was on file in the application as of June 17, 2002. In that regard, Applicants note that the Notification of Missing Requirements mailed in the present application on June 4, 2002 acknowledges receipt of the Information Disclosure Statement. Applicants are not aware of any requirement that an Applicant withhold an Information Disclosure Statement until all §371 requirements have been met, as the Examiner seems to be indicating. Accordingly, it is Applicants' position that the Examiner "shall" consider the timely filed Information Disclosure Statement in accordance with 37 C.F.R. §1.97. At this time, therefore, Applicants respectfully request that the previously submitted IDS be considered and that the Examiner acknowledge consideration of the references included therein in the next communication. If the Examiner remains of the opinion that the IDS cannot be considered, Applicants respectfully request that the Examiner direct attention to authority supporting such a position.

Examiner's rejection under 35 U.S.C. §112, first paragraph, written description

The Examiner rejected claims 63-65, 69-70, and 72-75 under 35 U.S.C. §112, first paragraph, as lacking adequate written description. The Examiner's full rationale is set forth in detail at pages 3-9 of the Office Action. Essentially, the Examiner has taken the position that the claims lack adequate written description because the specification fails to describe with any

structural specificity a representative number of inhibitors of ANT-1, or variant ANT-1 proteins, or describe the signal pathway being activated by ANT-1. According to the Examiner, the specification thus fails to describe "structural features common to the genus, which features constitute a substantial portion of the genus." Moreover, in the Examiner's opinion, the specification also lacks disclosure of sufficiently detailed identifying characteristics, such as complete or partial structure (of the inhibitor), other physical or chemical properties, or characteristics of inhibitors that would indicate a correlation between structure and function. The Examiner acknowledges a description of the ANT-1 inhibitors cyclophilin D and bongkrekic acid, but asserts that these are insufficient to provide description of the entire claimed genus. The Examiner has stated that these would not constitute a representative number of species of substances that inhibit the activity of ANT-1 or of ANT-1 protein antagonists because they do not share a common structural feature with each other and because the specification does not disclose common structural features among the broadly claimed genus of ANT-1 inhibitors. The Examiner also has asserted that even though the structure of ANT-1 is known, one would not be able to predict inhibitors of its activity, particularly in light of the fact that ANT-1's three dimensional structure is not disclosed or known.

In response, without conceding the correctness of the Examiner's position, but to expedite allowance of the application, Applicants have amended claims 63 and 73 to recite that the inhibitors employed in the claimed method interact directly with ANT-1. The specification, particularly at page 5, paragraph 2 describes such inhibitors and how one would identify.

Moreover, Applicants have added new claims 94 and 95 that further define the interaction as comprising binding the N-terminal domain of ANT-1. Accordingly, the method of apoptosis inhibition recited in the claims is adequately described and thus, Applicants respectfully request reconsideration and withdrawal of the rejection of claims 63-65, 69-70, and 72-75 under 35 U.S.C. §112, first paragraph (written description).

Examiner's rejection under 35 U.S.C. §112, first paragraph, written description

The Examiner rejected claims 63-65, and 69-75 under 35 U.S.C. §112, first paragraph, as allegedly failing to comply with the enablement requirement. The Examiner's rationale is set forth in detail at pages 10-20 in the Office Action. The Examiner has first asserted that the application improperly incorporates essential material (ANT-1) by reference and has indicated that the specification will need to be amended to include this material.

The substance of the Examiner's enablement rejection essentially relies on an assertion that the *in vitro* inhibition of ANT-1 induced apoptosis by cyclophilin D does not reasonably correlate with, and is not reasonably predictive of *in vivo* inhibition or treatment of any particular disease associated with such induction. The Examiner further asserted that one could not predict that an inhibitor of the ADP/ATP exchange activity of ANT-1 could be used for inhibiting apoptosis because ANT-1 apoptosis activity does not depend on ADP/ATP exchange.

In response, Applicants respectfully traverse the Examiner's rejection. Applicants' claimed invention is directed to, *inter alia*, a method for the inhibition of apoptosis, comprising contacting a cell associated with excessive apoptosis with an effective amount of a substance

capable of inhibiting the activity of adenine nucleotide translocase-1 (ANT-1) by direct interaction with ANT-1, and to a method for the treatment of diseases associated with excessive apoptosis, comprising the step of administering to a subject in need thereof a pharmaceutically effective amount of a substance capable of inhibiting the activity of adenine nucleotide translocase (ANT-1) by direct interaction with ANT-1.

Applicants first attach hereto the amino acid sequence of ANT-1 (NP-001142.2) and its corresponding DNA sequence (NM-001151.2). Applicants note that ANT-1 was a well-known polypeptide at the time the present application was filed. In that regard, Applicants attach hereto a publication by Neckelmann, et al., dated November 19, 1987, in which the ANT-1 amino acid sequences are indicated. One of ordinary skill in the art would have readily recognized, from the art, the ANT-1 recited in the claims and therefore would have readily been able to practice the methods claimed by following the teachings set forth in the specification. In any event, if the Examiner requires that the known sequence information be specifically inserted into the specification and an appropriate accompanying affidavit submitted as suggested in the Office Action, Applicants will consider providing such amendment and affidavit upon a specific request by the Examiner.

Applicants also attach hereto experimental data demonstrating inhibition of ANT-1 induced apoptosis by bongkrekic acid. These data, along with the additional documents attached hereto demonstrate that the claims, as amended, are fully enabled by the specification. One of ordinary skill in the art would readily be able to practice the claimed invention, and would

recognize that the data presented herein sufficiently correlate with the method claims, as presently amended. Accordingly, Applicants respectfully request that the Examiner reconsider and withdraw the rejection of the claims under 35 U.S.C. §112, first paragraph (enablement).

Examiner's rejection under 35 U.S.C. §102(b)

The Examiner rejected claims 63-65, 69-70, and 72 under 35 U.S.C. §102(b) as allegedly being anticipated by Fulda, et al. *Cancer Res.* 1998, 58(19): 4453-60, already of record. According to the Examiner, Fulda teaches that apoptosis in neuroblastoma cells is inhibited by bongkrekic acid, an agent that stabilizes mitochondria membrane barrier function. The Examiner's position is that the method taught by Fulda comprises the same steps as the claimed method in that the method involves contacting "a cell" with an ANT-1 inhibitor and bongkrekic acid is such an inhibitor (as taught by Pei). In the Examiner's view, the method of Fulda would therefore inherently lead to the claimed inhibition of an apoptosis-inducing signal transduction pathway that is activated by ANT-1. Applicants note that the Examiner has not included claims 71 and 73-75 in this rejection, thus indicating that those specific embodiments apparently are free of the prior art.

In response, without conceding the correctness of the Examiner's position, but to expedite allowance of the subject application, Applicants have amended claim 63 to recite that the cell is a cell associated with excessive apoptosis. The neuroblastoma cells referred to in the Fulda, et al. reference are not cells associated with excessive apoptosis and thus, the Fulda publication does not anticipate Applicants' claims, as amended. Accordingly, Applicants respectfully request that

the Examiner reconsider and withdraw the rejection of claims 63-65, 69-70, and 72 under 35 U.S.C. §102(b).

In view of the above remarks and amendments to the claims, Applicants believe that the Examiner's rejections set forth in the September 15, 2005 Office Action have been fully addressed and that the present claims fully satisfy the patent statutes. Applicants therefore believe that the application is in condition for allowance. The Examiner is invited to telephone the undersigned if it is deemed to expedite allowance of the application.

Respectfully submitted,

December 15, 2005 By _____

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Attachments: Amino acid and DNA sequences of ANT-1
Neckelmann, et al. publication
Experimental data

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